LOW LEVEL OF BASELINE RESISTANCE TO INTEGRASE INHIBITORS L731,988 AND L870,810 IN RANDOMLY SELECTED SUBTYPE B AND NON-B HIV-1 STRAINS

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BACKGROUND
HIV-1 reverse transcriptase (RT) and/or integrase (IN) inhibitors are currently in phase II or III clinical trials. A major concern is the emergence of resistance mutations in the viral genome, which may render these agents ineffective against infections. The effect of naturally occurring polymorphisms in the IN gene on susceptibility to L731,988 and L870,810 was investigated using a recombinant assay. A resistance assay was performed by transfecting 293T cells with recombinant virus stocks containing the RT-IN chimeric transgene (RT-IN chimera), which was amplified from the cloned SIV gag gene and inserted into pNL4-3 (+) or R5-HIV-1. The resulting recombinant virus was used to infect the 293T cells, and the susceptibility of the resulting 293T-RT-IN chimera cells to L731,988 and L870,810 was determined by limiting dilution. The IC50 values for each virus were determined by nonlinear regression analysis.

RESULTS

- A total of 60 patient samples, including 50 HIV-1 subtype B and 10 non-B subtype B, were selected for further genotypic and phenotypic analysis.
- The IC50 values for wild-type HIV-1 and FC values for each inhibitor were determined for each patient sample.
- The susceptibility of the RT-IN chimera cells to L731,988 and L870,810 was determined by limiting dilution. The IC50 values for each virus were determined by nonlinear regression analysis.
- The IC50 values for wild-type HIV-1 and FC values for each inhibitor were determined for each patient sample.

CONCLUSIONS

- The IC50 values for wild-type HIV-1 and FC values for each inhibitor were determined for each patient sample.
- The susceptibility of the RT-IN chimera cells to L731,988 and L870,810 was determined by limiting dilution. The IC50 values for each virus were determined by nonlinear regression analysis.
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REFERENCES